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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,298	12/21/2001	Toshihiko Yanagita	YAM 2 0014	9018

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,298	YANAGITA, TOSHIHIKO	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-15-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-24-05 has been entered.

2. The amendment filed, 1-24-05, is hereby acknowledged. Claims 3-6 and 8-10 were amended. Claims 1-15 are pending in this application.

3. All rejections made in the previous office action and not cited herein are hereby withdrawn. New Grounds for rejections follow below.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claim 1-10 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yallampalli et al. (WO9734922) for the reasons set forth below and the reasons set forth in the previous office action.

The claims are drawn to method of preventing premature labor or miscarriage using a composition comprising adrenomedullin.

Applicants argue that homology between AM and CGRP or active sites is about 25% and their respective expression levels differ in different organs. Further, their effects are different despite belonging to the same protein family. "Thus, even if Yallampalli, et al. discloses the effects of CGRP, it could not be said that Yallampalli et al. discloses the effect of AM on spontaneous myomaterial contraction or bradykinin induced contraction."

Applicants arguments filed, 1-25-05, have been fully considered but have not been found persuasive.

The reference teaches the prevention of preterm labor using adernomedullin peptide. The reference discloses that to a human female with signs and symptoms of preeclampsia or eclampsia of pregnancy or preterm/premature labor, 0.1-0.5 nmol/kg/24 hr doses of CGRP or CGRP/adrenomedullin peptide or receptor-based analogues should be administered in equivalent doses with or without supplementation with a progestin, a NO substrate or donor (see paragraph bridging page 2-3 and 19, lines 21-56). Applicants have only focused on the administration of CGRP and the fact that CGRP has only a 25% homology with AM. However, the reference discloses the administration of both CGRP and adrenomedullin. The administration of adernomedullin to the pregnant woman susceptible to premature/preterm labor would inherently result in a method of inhibiting spontaneous myometrial contraction or bradykinin induced contraction.

The rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claim 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yallampalli et al. (WO9734922) as applied to claims 1-10 above, and further in view of Kitamura et al (US5639855) for the reasons set forth in the previous office action and the reasons set forth below.

The claims are drawn to method of preventing premature labor or miscarriage using a composition comprising adrenomedullin.

Applicants argue that the mechanism of AM differs from that of CGRP. "AM could inihibt abnormal myometrial contraction via inflammatory mediator such as bradykinin, not myometrial contraction by PGF2α as seen in normal labor. CGROP does not have such an effect. In fact, Yallampalli, et al. indicates that CGRP only inhibits myometrial contractions in the later term of pernfancy (Day 18) and thus might inhibit normal labor. However, AM of the present invention does not inhibit contraction by PGF2α, oxytocin or the like and therefore does not inhibit normal labor." The secondary reference does not teach a method for spontaneous myometrial contractions or bardykinin induced contractions. Thus, the reference combined do not render obvious the claimed invention.

Applicants arguments filed, 1-25-05, have been fully considered but have not been found persuasive.

The reference of Yallampalli et al. teaches the prevention of preterm labor using adernomedullin peptide. The reference discloses that to a human female with signs and symptoms of preeclampsia or eclampsia of pregnancy or preterm/premature labor, 0.1-0.5 nmol/kg/24 hr doses of CGRP or CGRP/adrenomedullin peptide or receptor-based analogues should be administered in equivalent doses with or without supplementation with a progestin, a NO substrate or donor (see paragraph bridging page 2-3 and 19, lines 21-56). Applicants have only focused on the administration of CGRP and the fact that CGRP has only a 25% homology with AM. However, the reference discloses the administration of both CGRP and adrenomedullin. The administration of adernomedullin to the pregnant woman susceptible to premature/preterm labor would inherently result in a method of inhibiting spontaneous myometrial contraction or

bradykinin induced contraction. Applicants have argued mechanism involved in the claimed invention. However, the claims state "method of inhibiting spontaneous myometrial contractions." The claimed limitation is met when the reference discloses the treatment of spontaneous contractions regardless of how they are induced. Thus, it is inconsequential if the contractions were induced by bradykinin or PGF2α.

The rejection is maintained.

New Grounds For Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims state "[a] method of claim 1 or 2, wherein the adrenomedullin is. . ." The claims then go on to define adreonmedullin as a peptide comprising an amino acid sequence having one or several amino acid deleted, substituted or added to the fragments claimed. However these are not defined as adrenomedullin but are defined as adrenomedullin deletion analogs or adrenomedulllin analogs. It is well known in the art that human adrenomedullin is a 52 amino acid peptide and rat adrenomedullin is a 50 amino acid peptide that have specific sequences. One would not defined adrenomedullin as a peptide that has significant addition, deletion of amino acids with respect to the

native. These would be classified as adrenomedullin analogs. Thus, the definition of adrenomedullin recited in the claims is inconsistent with what is conventionally known in the art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 1, 7-10 remain rejected under 35 U.S.C. 102(b) as being anticipated by Sameulson et al.

The claims are drawn to method of preventing premature labor or miscarriage using a composition comprising adrenomedullin that has several amino acid deletions.

Sameulson et al. teach calcitonin gene related peptide (CGRP) and its usefulness in inhibiting spontaneous contraction (see abstract). The reference states that CGRP is a potent inhibitor of spontaneous contractile activity in the oviduct and uterus (see page 229). CGRP reads on the claimed invention because CGRP is a deletion analog of adrenomedullin. Since the claims allows for "several amino acid" deletions, CGRP meets the limitation of claims.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campbell, can normally be reached on (571) 272-0974. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

3/13/05

Anish Gupta
Patent Examiner